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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

Ex parte JOSEPH FISHER, JAMES LORENS,
DONALD PAYAN, and ALEXANDER ROSSI

Appeal 2012-008150
Application 09/293,670[1]
Technology Center 1600

Before DEMETRA J. MILLS, FRANCISCO C. PRATS, and
MELANIE L. McCOLLUM, Administrative Patent Judges.

PRATS, *Administrative Patent Judge*.

DECISION ON APPEAL

This appeal under 35 U.S.C. § 134 involves claims to a method for screening cells. The Examiner entered rejections for new matter, lack of written description, lack of enablement, and obviousness.

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[1] This application has been before us on appeal previously, as Appeal No. 2009-015210. A decision affirming rejections for obviousness was entered on July 21, 2010.

We have jurisdiction under 35 U.S.C. § 6(b). We reverse.

STATEMENT OF THE CASE

Claims 37-44 stand rejected and appealed (App. Br. 3).[2] Claim 37, the only independent claim, illustrates the appealed subject matter and reads as follows:

> 37. A method, comprising:
>
> introducing a library of at least 10^3 vectors encoding different candidate agents into a population of mammalian cells grown *in vitro*;
>
> subjecting the population of cells to a physiological signal, wherein said physiological signal stimulates a phenotype in said cells in the absence of the candidate bioactive agents;
>
> sorting the individual cells in the population on the basis of at least three optical properties by fluorescent activated cell sorting (FACS),
>
> identifying a cell having a phenotype that is altered relative to other cells in the population; and
>
> sequencing the nucleic acid encoding said candidate agent in said cell that has an altered phenotype, thereby identifying said candidate agent in said cell.

The following rejections are before us for review:

(1) Claims 37-44, under 35 U.S.C. § 112, first paragraph, as reciting new matter (Ans. 6-12);

(2) Claims 37-44, under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement (Ans. 12-14);

(3) Claims 37-44, under 35 U.S.C. § 112, first paragraph, as lacking enablement for the full scope of the subject matter claimed (Ans. 14-17);

(4) Claims 37 and 40-44, under 35 U.S.C. § 103(a) as obvious over Nolan,[3] Jia-ping,[4] and Uhr[5] (Ans. 18-22); and

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[2] Appeal Brief entered November 22, 2011.

(5) Claims 38 and 39, under 35 U.S.C. § 103(a) as obvious over Nolan, Jia-ping, Uhr, and Hide[6] (Ans. 22-23).

NEW MATTER

In rejecting claims 37-44 as containing new matter, the Examiner found that, "[c]laim 37 in its entirety is not supported in the as-filed specification" (Ans. 6). The Examiner found that the portions of the Specification cited by Appellants as describing the claimed process did not adequately support claim 37 (*id.* at 6-12), reasoning in particular that "the disparate sections cited by applicants do not lend support for the present [amended] claims" (*id.* at 12).

Instead, the Examiner contended, claim 37 "in its entirety should appear in the specification as in the claim. Picking and choosing disparate sections in the specification to support the individual element of the claims leads to a claim that is loosely connected and as the elements themselves do not find support in the as-filed specification" (*id.*).

As our reviewing court explained in *In re Oetiker*, 977 F.2d 1443, 1445 (Fed. Cir. 1992):

> [T]he examiner bears the initial burden . . . of presenting a *prima facie* case of unpatentability. . . .
>
> After evidence or argument is submitted by the applicant in response, patentability is determined on the totality of the

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[3] WO 97/27212 A1 (published July 31, 1997).
[4] Tao Jia-ping et al., *Multi-parameter sorting technique in flow cytometry*, 17 CHINESE JOURNAL OF PHYSICAL MEDICINE 168-171 (1995).
[5] U.S. Patent No. 5,612,185 (issued March 18, 1997).
[6] Izumi Hide et al., *Degranulation of Individual Mast Cells in Response to Ca^{2+} and Guanine Nucleotides: An All-or-None Event*, 123 J. CELL BIOL. 585-593 (1993).

> record, by a preponderance of evidence with due consideration to persuasiveness of argument.

As the Federal Circuit also explained in *TurboCare Div. of Demag Delaval Turbomachinery Corp. v. General Elec. Co.*, 264 F.3d 1111, 1118 (Fed. Cir. 2001):

> The written description requirement and its corollary, the new matter prohibition of 35 U.S.C. § 132, both serve to ensure that the patent applicant was in full possession of the claimed subject matter on the application filing date. When the applicant adds a claim or otherwise amends his specification after the original filing date . . ., the new claims or other added material must find support in the original specification.

Nonetheless, "[i]n order to satisfy the written description requirement, the disclosure as originally filed does not have to provide *in haec verba* support for the claimed subject matter at issue." *Purdue Pharma L.P. v. Faulding, Inc.*, 230 F.3d 1320, 1323 (Fed. Cir. 2000).

Rather, the "test for sufficiency is whether the disclosure of the application relied upon reasonably conveys to those skilled in the art that the inventor had possession of the claimed subject matter as of the filing date." *Ariad Pharmaceuticals, Inc. v. Eli Lilly and Co.*, 598 F.3d 1336, 1351 (Fed. Cir. 2010).

Beyond simple possession, however, the "test requires an objective inquiry into the four corners of the specification from the perspective of a person of ordinary skill in the art. Based on that inquiry, the specification must describe an invention understandable to that skilled artisan and show that the inventor actually invented the invention claimed." *Id.*

In this instance, we agree with Appellants that the preponderance of the evidence does not support the Examiner's finding that the Specification fails to adequately describe the process recited in claim 37.

As Appellants point out, the general method recited in claim 37 is initially described at page 4 of the Specification:[7]

> The methods generally comprise combining at least one candidate bioactive agent and a population of cells, sorting the cells in a FACS machine by separating the cells on the basis of at least three, four or five cellular parameters. The candidate agents can be part of a molecular library comprising fusion nucleic acids encoding the candidate bioactive agents.

(Spec. 4.)

The Specification also discloses that a "population of cells" means at least 10^3 cells (*id.* at 10), and that, when nucleic acid vectors such as retroviral vectors are used as the candidate bioactive agents, each cell in the population receives a distinct construct (*see id.* at 19-21; App. Br. 9). We acknowledge that preferred embodiments of the described process use a library of vectors with at least 10^6 different sequences (*see id.* at 19). However, given the disclosure of using cell populations of at least 10^3 cells, each of which receives a distinct construct, i.e., one cell receives at least one vector, we agree with Appellants that the Specification adequately describes introducing a library of at least 10^3 vectors to those cells, as recited in claim 37.

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[7] Appellants and the Examiner both appear to cite to pages of the Specification as originally filed on April 16, 1999. We do the same for consistency.

Similarly, given the Specification's express disclosure that the described method may include evaluation of the cells' reaction to the bioactive agents in the presence of a physiological signal such as a hormone, antibody peptide, cytokine, growth factor, etc. (Spec. 9-10), we agree with Appellants that the Specification necessarily describes claim 37's step of subjecting the cells to a physiological signal. Also, because the FACS technique sorts on the basis of optical properties, we agree with Appellants that an ordinary would understand that sorting cells based on at least three, four, or five cellular parameters (*see* Spec. 4) would in effect describe sorting on the basis of at least three optical parameters, as recited in claim 37.

We acknowledge that the Specification does not explicitly state that the nucleic acid sequence of the vector encoding the bioactive agent is determined, as required by claim 37. However, we agree with Appellants that a disclosure of analyzing the structure of the bioactive agent in a manner "appreciated by those in the art" (Spec. 43) would lead an ordinary artisan to understand that the sequence would be determined when the agent is encoded by a nucleic acid. *Cf. Purdue Pharma v. Faulding,* 230 F.3d at 1323 ("Put another way, one skilled in the art, reading the original disclosure, must immediately discern the limitation at issue in the claims.").

Thus, the Specification initially describes a general process as recited in claim 37, and subsequently describes the steps of claim 37's process as being preferred features of that general process. We therefore agree with Appellants that a preponderance of the evidence does not support the Examiner's finding that the overall process recited in claim 37 lacks

adequate descriptive support. Accordingly, we reverse the Examiner's new matter rejection of claim 37 and its dependent claims.

WRITTEN DESCRIPTION

In rejecting claims 37-44 for lack of written description, the Examiner found that, "[s]ince there is no description of a library of [10^3] vectors hence, there is no description of a candidate agent that has been isolated or identified by the encoded diverse library of [10^3] vectors where the candidate agents alter a phenotypic change to a population of mammalian cells" (Ans. 13). The Examiner also found that the Specification does not exemplify a process as claimed, since the "working example in the specification describes the effect of a single known candidate agent p21 and its phenotypic effect to a population of [10^3] cells. There is no description of whether the single known p21 has been selected, purified and identified from the [10^3] library of vectors" (*id.* at 13-14).

The Examiner further found:

> Nor is there a description of an isolated and identified candidate agent that alters any or all kind(s) of phenotypes in a population of cell. Since no identification of a candidate peptide agent has been made and the single protein (not peptide) is known hence, it is not readily apparent how sequencing can be done to an already known protein.

(*Id.* at 14.)

We agree with Appellants that the preponderance of the evidence does not support the Examiner's finding that the claims lack descriptive support. As the Federal Circuit has noted:

> A claim will not be invalidated on section 112 grounds simply because the embodiments of the specification do not

> contain examples explicitly covering the full scope of the claim language. That is because the patent specification is written for a person of skill in the art, and such a person comes to the patent with the knowledge of what has come before. Placed in that context, it is unnecessary to spell out every detail of the invention in the specification; only enough must be included to convince a person of skill in the art that the inventor possessed the invention and to enable such a person to make and use the invention without undue experimentation.

Falkner v. Inglis, 448 F.3d 1357, 1366 (Fed. Cir. 2006) (quoting *LizardTech, Inc. v. Earth Resource Mapping, PTY, Inc.*, 424 F.3d 1336, 1345 (Fed.Cir.2005)).

In the instant case, in contrast to claims requiring a specific therapeutic compound unknown in the prior art and structurally undefined in the Specification, as was the case for example in *Univ. of Rochester v. G.D. Searle & Co.*, 358 F.3d 916, 922 (Fed. Cir. 2004), the process of claim 37 is a screening method which, by its nature, seeks to identify a phenotype-altering agent from the library of candidate agents encoded by nucleic acid vectors.

While the Examiner urges that the library of vectors has not been described, as noted above in *Falkner*, exemplification is not necessary where an ordinary artisan would understand that Appellants possessed the process as claimed. As Appellants point out, the Specification explains, with significant specificity, the nature of nucleic acid vector libraries useful in the disclosed process, including a focus on retroviral libraries (*see* Spec. 19-21). In contrast, the Examiner has not advanced any persuasive evidence specifically suggesting that an ordinary artisan would have failed to be

convinced, based on that disclosure, that Appellants invented a screening process that included the use of such libraries.

We are therefore not persuaded that a preponderance of the evidence supports the Examiner's finding that Appellants did not possess the screening method recited in claim 37. Accordingly, we reverse the Examiner's written description rejection of that claim, and its dependents.

ENABLEMENT

The Examiner rejected claims 37-44 under 35 U.S.C. § 112, first paragraph, because the Specification, "while being enabling for a method using a single protein, does not reasonably provide enablement for claim 37 method using a library of [10^3] vectors and the other claim parameters (as given in the new matter rejection above)" (Ans. 14).

The Examiner reasoned that, because the Specification provided "only broad generalized statements," an ordinary artisan would have to undertake an "undue amount of experimentation to determine the [10^3] library of vectors encoding different candidate agents that alters any type of phenotype in a cell(s) population. This is made more complex since the specification does not provide support for the claim[ed] general method. (Please see the new matter rejection above.)" (*Id.* at 15.) As evidence of unpredictability in the art, the Examiner cited Polyak,[8] Nakanishi,[9] and Tournier[10] (*id.* at 16-17).

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[8] Kornelia Polyak et al., *Genetic determinants of p53-induced apoptosis and growth arrest*, 10 GENES & DEVELOPMENT 1945-52 (1996).
[9] Makoto Nakanishi et al., *Identification of the active region of the DNA synthesis inhibitory gene p21*$^{Sdi1/CIP1/WAF1}$, 14 THE EMBO JOURNAL 555-563 (1995).

We conclude that a preponderance of the evidence does not support the enablement rejection.

As noted in *Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d 1313, 1334 (Fed. Cir. 2003):

> The enablement requirement is often more indulgent than the written description requirement. The specification need not explicitly teach those in the art to make and use the invention; the requirement is satisfied if, given what they already know, the specification teaches those in the art enough that they can make and use the invention without "undue experimentation."

Moreover, "[working] examples are not required to satisfy section 112, first paragraph." *In re Strahilevitz*, 668 F.2d 1229, 1232 (CCPA 1982). For example, in *Falkner v. Inglis*, the court affirmed the conclusion of the Board of Patent Appeals and Interferences, that claims to a modified pox virus vaccine were enabled, despite the fact that the specification focused on viruses other than pox virus, provided no examples directed to pox virus, and discussed pox virus only in general terms relating to the inventive disclosure. *Falkner,* 448 F.3d at 1365.

Also, significant experimentation does not preclude enablement:

> Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. . . . The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question

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[10] Sylvie Tournier, *Heterologous Expression of the Human Cyclin-dependent Kinase Inhibitor p21^{Cip1} in the Fission Yeast, Schizosaccharomyces pombe Reveals a Role for PCNA in the chkl+ Cell Cycle Checkpoint Pathway*, 7 MOLECULAR BIOLOGY OF THE CELL 651-662 (1996).

> provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed.

In re Wands, 858 F.2d 731, 736-37 (Fed. Cir. 1988) (citations omitted).

In this case, the process recited in claim 37 is a screening method, which by its nature includes a substantial degree of unpredictability, since the outcome of the screening procedure is not assured. Similarly, an ordinary artisan would understand that screening methods, because of their nature, involve significant amounts of experimentation. Thus, while it may be true that Polyak, Nakanishi, and Tournier suggest that understanding cell cycle regulation can present significant problems, the point of the claimed method is to study such processes by ascertaining molecules that can affect them.

We acknowledge that the claimed screening method may require a significant number of repetitions to obtain any useful result. However, as noted above, the claim is limited to screening a population of cells using a library of nucleic acid vectors, a known class of molecules, and the Specification describes, with reference to the prior art, techniques by which those molecules can be obtained (*see* Spec. 19-20). In contrast, the Examiner has not advanced any specific evidence clearly suggesting that an ordinary artisan, equipped with what was already known about generating libraries of nucleic acid vectors, would have been unable to practice the claimed invention based on the teachings provided in the Specification.

Thus, as we are not persuaded that a preponderance of the evidence supports the Examiner's conclusion that practicing the full scope of claim 37 would necessitate undue experimentation, we reverse the Examiner's rejection of claim 37 and its dependents for lack of enablement.

OBVIOUSNESS

In concluding that the process recited claims 37 and 40-44 would have been obvious to an ordinary artisan viewing Nolan, Jia-ping, and Uhr, the Examiner reasoned that the artisan would have been prompted to "determine the changes in the exocytosis phenotype of a cell by at least 3 optical parameters in the method of Nolan in the manner as taught by Jia-ping and Uhr . . . for the advantages taught by Jia-ping and Uhr" (Ans. 21-22).

In concluding that the processes recited in dependent claims 38 and 39 would have been obvious over Nolan, Jia-ping, Uhr, and Hide, the Examiner further reasoned that an ordinary artisan would have been prompted to "use stimulus as Ca++ or ionomycin to differentiate one cell from another by the effect of the stimulus. One would have a reasonable expectation of success since exocytosis phenotype has been used to differentiate cells in a population using FACS" (*id.* at 23).

Appellants do not allege error in either the Examiner's fact findings or the ultimate conclusions of obviousness drawn from them. Instead, Appellants argue only that the Nolan reference is not prior art with respect to the instant application as evidenced by the Fisher Declaration[11] (App. Br. 23-25).

Specifically, Appellants argue, the instant application claims priority to an application (09/062,330) filed less than one year after the publication date of the Nolan reference, and the Nolan reference is therefore available as prior art to the instant application only under 35 U.S.C. § 102(a) (*id.* at 24). Thus, Appellants urge, because the Fisher Declaration filed under 37 C.F.R.

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[11] Declaration of Joseph Fisher under 37 C.F.R. § 1.131 (executed June 25, 2006).

§ 1.131 establishes invention of the subject matter in the rejected claims prior to the publication date of Nolan, Nolan is not available as prior art against the rejected claims (*id.* at 24-25).

The Examiner does not dispute that the Fisher Declaration is adequate to support invention of the claimed subject matter prior to the July 31, 1997 publication date of the Nolan reference. Rather, the Examiner argues that the '330 application[12] fails to provide adequate descriptive support for the process recited in the rejected claims.

In particular, the Examiner notes that the '330 application's disclosure is limited to "screening for alterations in **exocytosis of a population of cells (not the now presently broad claimed physiological signal)**" (Ans. 45). As to the specific features of the claimed process, the Examiner states that "the responses above under the new matter rejection are incorporated herein in its entirety. The cited section as support, for example, for library of [10^3] vectors in the parent application is no different from the instant application" (*id.* at 46).

We agree with Appellants that the preponderance of the evidence does not support the Examiner's finding that the '330 application fails to provide adequate descriptive support for the claimed process.

We initially note, as the Examiner contends, that the disclosure of the '330 application is very similar to that of the instant application. Thus, the '330 application initially describes a general method of screening cells by

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[12] This application is a continuation in part of 09/157,748, filed September 21 (now U.S. Patent No. 6,461,813), which is in turn a continuation in part of 09/062,330, filed April 17, 1998 (now U.S. Patent No. 6,897,031).

FACS to select introduced agents that alter phenotypic traits characteristic of exocytosis:

> In accordance with the objects outlined above, the present invention provides a method for screening for alterations in exocytosis of a population of cells or in single cells under different conditions or combined with different bioactive agents. The methods comprise sorting the cells in a FACS machine by assaying for alterations in at least three of the properties selected from the group consisting of light scattering, fluorescent dye uptake, fluorescent dye release, annexin granule binding, surface granule enzyme activity, and the quantity of granule specific proteins.

('330 Spec. 3.) Like the instant application, the '330 application discloses that a "population of cells" means at least 10^3 cells (*id.* at 24), and that, when nucleic acid vectors such as retroviral vectors are used as the candidate bioactive agents, each cell in the population receives a distinct construct (*see id.* at 24-26).

We acknowledge that preferred embodiments of the process described in the '330 application use a library of vectors with at least 10^6 different sequences (*see id.* at 24). However, given the disclosure of using cell populations of at least 10^3 cells, each of which receives a distinct construct, just as described in the instant application, we agree with Appellants that the '330 application adequately describes introducing a library of at least 10^3 vectors to that population of cells, as recited in claim 37.

Similarly, given the '330 application's express disclosure that the described method may include evaluation of the cells' reaction to the bioactive agents in the presence of a physiological signal such as a hormone, antibody peptide, cytokine, growth factor, etc. ('330 Spec. 8), we agree with Appellants that the '330 application necessarily describes claim 37's step of

subjecting the cells to a physiological signal that stimulates a phenotype in the cells. Also, because the '330 application describes FACS sorting on the basis of "at least three of the properties selected from the group consisting of light scattering, fluorescent dye uptake, fluorescent dye release, annexin granule binding, surface granule enzyme activity, and the quantity of granule specific proteins" (*id.* at 3), we agree with Appellants that the sorting step in claim 37 is adequately described in the '330 application.

We also acknowledge that the '330 application does not explicitly state that the nucleic acid sequence of the vector encoding the bioactive agent is determined, as required by the final step of claim 37. However, we agree with Appellants that a disclosure of analyzing the structure of the bioactive agent as "appreciated by those in the art" ('330 Spec. 40) would lead an ordinary artisan to understand that the sequence would be determined when the agent is encoded by a nucleic acid.

Thus, like the instant Specification, the '330 application initially describes a general process as recited in claim 37, and subsequently describes the steps of claim 37's process as being preferred features of that general process. We therefore agree with Appellants that a preponderance of the evidence does not support the Examiner's finding that the processes recited in claim 37 and its dependents lack adequate descriptive support in the '330 application.

Accordingly, as a preponderance of the evidence does not support the Examiner's finding that the claimed process is not entitled to priority to the '330 application, and as the Examiner does not dispute that the Fisher Declaration adequately demonstrates invention of the claimed process prior to the Nolan reference, we reverse the Examiner's obviousness rejection of

claims 37 and 40-44 over Nolan, Jia-ping, and Uhr, as well as the Examiner's rejection of claims 38 and 39 over Nolan, Jia-ping, Uhr, and Hide.

SUMMARY

We reverse the Examiner's rejection of claims 37-44, under 35 U.S.C. § 112, first paragraph, as reciting new matter.

We also reverse the Examiner's rejection of claims 37-44, under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement.

We also reverse the Examiner's enablement rejection of claims 37-44.

We also reverse the Examiner's obviousness rejection of claims 37 and 40-44 over Nolan, Jia-ping, and Uhr.

We also reverse the Examiner's obviousness rejection of claims 38 and 39 over Nolan, Jia-ping, Uhr, and Hide.

REVERSED

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